

### **REMARKS**

The Office Action mailed July 2, 2002 and the Advisory Action mailed November 11, 2002 have been received and carefully considered. Applicants appreciate the Examiner's comments regarding the Applicants' traversal of the restriction requirement and the withdrawn claims. Applicants believe the current amended claims and remarks below address the Examiner's remaining concerns.

In accordance with 37 C.F.R. §§ 1.97 and 1.98, and in compliance with the duty of disclosure set forth in 37 C.F.R. § 1.56, applicants are submitting herewith copies of the references listed on the attached Form PTO/SB/08A for consideration and to be made of record herein by the U.S. Patent and Trademark Office in the above-captioned application.

### **Objections**

Applicants thank the Examiner for noting Table 1 was presented in the application after Table 2. Applicants have requested that Table 1 be inserted on page 29 and deleted from page 52 to address this issue. Therefore, Applicants respectfully request that the USPTO withdraw the objection.

### **35 U.S.C. §103(a)**

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 22 and 23 were rejected under 35 U.S.C. § 103(a) as being obvious over Viner. (U.S. 5,760,049) as teaching "a method for controlling tobacco use and alleviating withdrawal symptoms due to the cessation of tobacco use." Applicants first note that amended claim 22 and 23 now utilize the language "consisting essentially of." Viner teaches that the primary components required to alleviate withdrawal symptoms include the use of both an acetylcholine receptor antagonist and an acetylcholine esterase reactivator. In contrast, Applicants claim a method for enhancing the effectiveness of a nicotine replacement therapy consisting essentially of nicotine and one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, and/or translation of the gene encoding CYP2A; and (iii) substances which delete all or a portion of the gene

encoding CYP2A, and optionally (c) one or more substances selected from the group consisting of substances which inhibit CYP2B6 activity, substances which inhibit transcription and/or translation of the gene encoding CYP2B6, or a combination thereof, wherein (a), (b), and (c) if present, are administered contemporaneously. In light of this amendment to the claim, one skilled in the art certainly would not be motivated by Viner to practice the claimed invention. The current claim language excludes the use of either an acetylcholine receptor antagonist or an acetylcholine esterase reactivator, whereas Viner teaches that alleviating withdrawal symptoms requires the use of both. (See for example, claim 1). Indeed Viner may be viewed as actually teaching away from the invention as presently claimed.

Applicants invention provides nicotine, which itself alleviates withdrawal symptoms. However due to nicotine's short half, until the present invention, one would have been required to deliver large and frequent doses of nicotine to prevent these withdrawal symptoms and control tobacco use. Applicants invention increases the half life of the nicotine by blocking its mechanism for its breakdown through the inhibition of CYP2A. This is in contrast to Viner.

The USPTO contends that Viner teaches "a method for controlling tobacco use and alleviating withdrawal symptoms due to the cessation of tobacco use." Viner does teach a method of controlling tobacco use. It is a method that requires the use of both an acetylcholine receptor antagonist and an acetylcholine esterase reactivator. Further, the USPTO cites claim 11, which is ultimately dependent from claim 1, which cites the use of "nicotine, muscarine, arecoline, lobeline, cotinine, kat, nikethamide, ethamivan, bethanechol, pilocarpine, and mixtures thereof. As such, the USPTO is stating that Viner teaches a composition for alleviating smoking that in the very least requires the following:

- (i) an acetylcholine receptor antagonist;
- (ii) an acetylcholine esterase reactivator; and
- (iii) nicotine, muscarine, arecoline, lobeline, cotinine, kat, nikethamide, ethamivan, bethanechol, pilocarpine or mixtures thereof.

The USPTO argues that one skilled in the art would review Viner and determine they should eliminate portions (i) and (ii) and selectively choose nicotine and pilocarpine from the disclosure to achieve the claimed invention. This is without the knowledge or any disclosure by Viner regarding the importance of CYP2A activity and its relationship to nicotine metabolism and smoking.

Further, Applicants have added new independent claim 36 which relates to a method for enhancing the effectiveness of a nicotine replacement therapy comprising administering to an individual in need of nicotine replacement therapy a therapeutically effective amount of nicotine and one or more substances which inhibit CYP2A activity wherein the substances which inhibit CYP2A activity is selected from methoxsalen, psoralen, tranlycypromine, coumarin, chromone, esculetin, phenelzine, paroxetine, selegiline and pargyline, *Hypericum* and extracts thereof, *Cichorium intybus* and extracts thereof, and *Bougainvillra spectabilis* and extracts thereof. Applicants point out the claim requires the use of nicotine and a substance which inhibit CYP2A activity. Additionally, the substance which inhibits the CYP2A activity are selected from methoxsalen, psoralen, tranlycypromine, coumarin, chromone, esculetin, phenelzine, paroxetine, selegiline and pargyline, *Hypericum* and extracts thereof, *Cichorium intybus* and extracts thereof, and *Bougainvillra spectabilis* and extracts thereof. The Examiner will kindly note that pilocarpine is not in the Markush group. Viner is silent with regard to the recited compounds which inhibit CYP2A.

New independent claims 38 and 39 address relate to the use of nicotine with substances which inhibit transcription, and/or translation of the gene encoding CYP2A; or substances which delete all or a portion of the gene encoding CYP2A. Viner is silent with regard to both.

Additionally, the USPTO contends that "...it is clear from Viner that he was aware of the fact that tobacco use is unhealthy and needs to be stopped." (See, Office Action page 4, paper 12). Applicants do not disagree. However, Applicants respectfully point out that the method which Viner uses to address this issue is manifestly different from the method of the claimed invention. Viner is directed to the use of compositions which effect acetylcholine receptors while the claimed invention is directed to compositions which effect CYP2A activity. The USPTO further contended that "Viner administers the same composition to a patient just as the invention does." (See, Office Action page 4, paper 12). As demonstrated above this is not the case. Applicants again point out that pilocarpine is no longer being claimed. Further, Applicants contend that even if it were, the fact that pilocarpine and nicotine could have been chosen from the ten possible stimulants of Viner and used together to achieve an embodiment of the disclosure does not render the invention obvious. Viner provides no discussion of CYP2A activity and therefore no motivation to alter this activity.

Alternatively, The USPTO argues that Applicants use of the word "comprising"

does not preclude the use of an acetylcholine receptor antagonist and an acetylcholine esterase reactivator. (See Office Action page 6, mailed November 23, 2001). Applicants respectfully point out that a claimed invention is properly interpreted through review of the specification. The present specification does not discuss the use of oximes to alter an acetylcholine receptors or an acetylcholine esterase just as Viner does not disclose or discuss CYP2A activity or means of altering its activity. The statutory standard of §103 is whether the invention, considered as a whole, would have been obvious to one of ordinary skill in the art, not whether it would have been obvious for one of ordinary skill in the art to try various combinations. *Akzo N.V. v. E.I. duPont de Nemours*, 1 U.S.P.Q.2d 1705, 1707 (Fed. Cir. 1987).

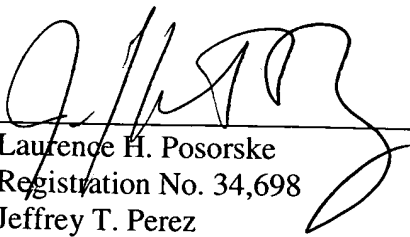
The rejections, to the extent applied against the claims as amended, are respectfully traversed.

#### CONCLUSION

Applicants assert that the above-referenced application is in condition for allowance. Reconsideration and allowance of all pending claims is respectfully requested. Should any outstanding issues remain, the Examiner is invited to telephone the undersigned at 202-955-1500.

Respectfully submitted,

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